## REMARKS

**Rejection under 35 U.S.C. § 102 – Anticipation**

The Examiner rejected claims 23-26, 30, 31, and 35-44 under 35 U.S.C. § 102(b) as being anticipated by PCT Publication No. WO 98/08503 to Kelly et al. (Kelly et al.); claims 23, 24, 28, 30, 31, and 33 under 35 U.S.C. § 102(b) as being anticipated by PCT Publication No. 98/25588 to Gorbach as evidenced by Setchell et al. (Setchell et al., *American Journal of Clinical Nutrition*, 2005); and 35 U.S.C. § 102(b) of claims 23, 24, 27, 30, 31 and 32 as being anticipated by U.S. Patent Publication No. 2004/0235758 to Setchell and Cole (Setchell and Cole).

At the outset, Applicants note independent claims 23 and 30. As amended, independent claim 23 is directed to a method of mediating androgen hormone action so as to ameliorate at least one condition of the prostate of a subject, the method including the step of administering equol, at least 1% of which is R-equol, wherein R-equol binds free 5α-dihydrotestosterone and inhibit its binding with androgen receptors. As amended, claim 30 is directed to a method of ameliorating at least one condition of the prostate of a subject, the method including administering equol, at least 1% of which is R-equol, wherein R-equol binds free 5α-dihydrotestosterone and inhibit its binding with androgen receptors.

Applicants also added independent claims 45-47. Claim 45 is directed to a method of mediating androgen hormone action so as to ameliorate benign prostatic hyperplasia, comprising administering equol in an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of 5α-dihydrotestosterone with the androgen receptors. Claims 46 is directed to a method co-mediating androgen hormone action and estrogen hormone action so as to ameliorate benign prostatic hyperplasia in a subject comprising administering equol in an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of the 5α-dihydrotestosterone

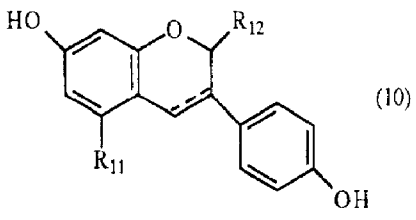
with the androgen receptors, and an amount sufficient to bind estrogen receptor subtypes. Claim 47 is directed to a pharmaceutical composition for ameliorating benign prostatic hyperplasia in a subject comprising equol in an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of 5α-dihydrotestosterone with the androgen receptors; and at least one of a pharmaceutically acceptable carrier, adjuvant, or excipient.

**The § 102 Rejection Based on Kelly et al. Should be Withdrawn.**

As stated in MPEP §2131:

> To anticipate a claim, the reference must teach each and every element of the claim." A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The Examiner's rejection does not meet these standards. The Kelly et al. reference does not teach, show or even suggest all of the elements of amended claims 23 and 30. Specifically, the Kelly et al. reference does not make any mention of enantiomers of equol and certainly do not teach, show or even suggest *administering compositions comprising equol, at least 1% of which being R-equol*. Applicants note that Kelly et al. list at least 20 different compounds at pages 1-5, including "compound 10," having the structure copied herein for the Examiner's convenience from the Kelly et al. reference, page 4.



(10)

The structure of "compound 10" includes two variable substituents, $R_{11}$ and $R_{12}$, which are defined as follows:

$R_{11}$ is H or OH,
$R_{12}$ is H, COOH, $CO_2R_C$ where $R_C$ and is as previously defined, or $CONHR_E$ where $R_E$ is as previously defined,

Clearly, "compound 10" of Kelly et al. is not a single compound but rather represents a general structure of several compounds. In fact, Kelly et al. refers to "compound 10" as "equol and dehydroequol," as seen in the below paragraph from page 6, lines 1-5:

Certain of the above compounds may be referred to by the names dihydrodaidzein (compound 1 where $R_8$ is H), dihydrogenestein (compounds 2 and 5), dehydro-O-desmethylangolensin (compound 11), tetrahydrodaidzein (compound 8), equol and dehydroequol (compound 10), O-desmethyl-angolensin (ODMA - compound 13), and 6-hydroxy-O-desmethylangolensin (6-hydroxy-ODMA - compound 14).

Also, when production of dehydroequol is discussed at page 28 of the Kelly et al. reference, dehydroequol is shown as including both compounds, dehydroequol and equol, without any indication of how much or each compound is present in the product. As such, it is unclear what in fact is even being referred to by Kelly et al. as "compound 10."

Applicants note that the structural differences between equol and dehydroequol are particularly significant in connection with the present invention. In particular, the two compounds differ by the inclusion of the double bond between carbons at positions 3 and 4 of the chroman ring in the dehydroequol. This inclusion of the double bond eliminates the chiral center otherwise present in equol. As such, one is left by Kelly et al. not knowing whether one had equol or dehydroequol or how much of either. As such, one would not have the invention defined by claims 23 and 30, which require a minimum percentage of R-equol.

For at least these reasons, the Kelly et al. reference does not anticipate Applicants' invention defined by claims 23 and 30, and any claims dependent therefrom. Applicants request that 35 U.S.C. § 102(b) rejection of claims 23-26, 30, 31, and 35-44 as being anticipated by to Kelly et al. be withdrawn.

**New Claims 45-47 are Likewise Not Anticipated by Kelly et al.**

Regarding newly added claims 45-47, Applicants note that Kelly et al. states that:

> "… compounds of formulae 1 to 19 [where compound 10 is identified as dehydroequol] have particular utility and effectiveness in the treatment, prophylaxis, amelioration defense against, and/or prevention of menopausal syndrome including hot flushes, anxiety, and depression, mood swings, night sweats, headaches, and urinary incontinence; osteoporosis; premenstrual syndrome, including fluid retension, cyclical mastalgia, and dysmenorrhoea; Reynaud's Syndrome; Reynaud's Phenomenon; Buergers Disease; coronary artery spasm; migraine headaches; hypertension, benign prostatic hypertrophy; breast cancer; uterine cancer; ovarian cancer; testicular cancer; large bowel cancer; endometrial cancer; prostatic cancer; uterine cancer; atherosclerosis; Alzheimers disease; inflammatory diseases including inflammatory bowel disease, ulcerative colitis, Crohns disease; rheumatic diseases including rheumatoid arthritis; acne; baldness including male pattern baldness (alopecia hereditaria); psoriasis and diseases associated with oxidant stress including cancer, myocardial infarction[,] stroke, arthritis, sunlight induced skin damage or cataracts."

Notwithstanding the inclusion of *benign prostatic hypertrophy* in this laundry list of various diseases (with varying pathological and clinical manifestations as well varying disease formation mechanisms) that may be treated, prevented or ameliorated with compounds of formulae 1-19, there is no specific teaching in the Kelly et al. reference that *equol* can 1) mediate androgen

hormone action so as to ameliorate benign prostatic hyperplasia, and 2) co-mediate androgen hormone actions and estrogen hormone action so as to ameliorate benign prostatic hyperplasia.

Even though in Example 10, Kelly et al. states that a group of patients suffering from benign prostatic hypertrophy and prostatic cancer of various grades was studied to determine the effects of compounds of the formulae 1 to 19, no specifics are provided about the patients, which compounds were given to which patients, any details about the design of the study. Importantly, no actual data were provided in Example 10.

The only other reference to benign prostatic hypertrophy provided in Example 10 relates to giving a single patient suffering from benign prostatic hypertrophy a specified amount of a *clover isoflavone containing extract* for an unspecified period of time. However, giving a patient a clover isoflavone containing extract is not the same as giving the patient equol. Equol would not be found in that extract. While it is true that equol is sometimes a metabolite from such an extract, this cannot be certain. As described, for example, at page 15, par. 100 of the instant application:

> "approximately 50-70% of the adult population did not excrete equol in urine even when challenged daily with soy foods … Furthermore, even when the pure isoflavone compounds are administered, thereby removing any influence of the food matrix, it has been shown that many people do not convert daidzein to equol."

Thus, one of skill in the art would understand that administering clover isoflavone containing extract to a patient is clearly not the same as administering equol.

As such, the Kelly et al. reference does not teach methods of mediating androgen hormone actions (claim 45) or co-mediating androgen hormone actions and estrogen hormone action (claim 46) as to ameliorate benign prostatic hypertrophy, the method including administering equol in an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of 5α-

dihydrotestosterone with the androgen receptors (claim 45), or an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of the 5α-dihydrotestosterone with the androgen receptors, and an amount sufficient to bind estrogen receptor subtypes (claim 46). In addition, Kelly et al. do not teach a pharmaceutical composition for ameliorating benign prostatic hyperplasia in a subject comprising equol in an amount sufficient to bind with free 5α-dihydrotestosterone, thereby inhibiting the binding of 5α-dihydrotestosterone with the androgen receptors; and at least one of a pharmaceutically acceptable carrier, adjuvant, or excipient.

**The § 102 Rejection Based on Gorbach as evidenced by Setchell et al. Should Also be Withdrawn.**

Similarly, the Gorbach reference does not teach, show or even suggest all of the elements of Applicants' independent claims 23 and 30. Specifically, the Gorbach reference does not make any mention of enantiomers of equol and certainly does not teach, show or even suggest c*ompositions comprising equol, at least 1% of which is R-equol*. The Gorbach reference refers simply to "equol," as one of a long list of isoflavonoids. However, it is unclear from the Gorbach reference what in fact is even being referred to. Applicants note the following disclosure, found at lines 6-11 at page 2 of the Gorbach reference:

> "Isoflavonoids which may be administered according to the invention include genistein, daidzein, biochanin A, formononetin, O-desmethylangolensin, glycitin, and equol; these may be administered alone or in combination. The isolated isoflavonoid may be administered in any suitable form, e.g., in the form of a plant extract rich in isoflavonoids or in the form of purified or synthesized isoflavonoid. By "isolated" is meant the isoflavonoid is in a form which is more concentrated than the form in which it occurs naturally in plants."

Notwithstanding the inclusion of equol among the above-listed isoflavonoids, no naturally-occurring plant derived source of equol is

known (equol is metabolized by bacterial flora from daidzein; see e.g., specification at page 2, par. 7). Moreover, even if the substance referred to as "equol" in the Gorbach reference was derived from plants, there would be no reason to believe it had a chiral center because the Gorbach reference makes no mention of the structure or chirality of equol (or any other compound referred to therein). More significantly, there would be no reason to believe that the S- and R- equol were taught by the Gorbach reference.

Because it was known at the time of filing of Gorbach that the naturally occurring form of equol is S-equol, a skilled artisan reading the Gorbach reference would understand that Gorbach teaches S-equol. See, for example, articles by L. Verbit and J.W. Clark-Lewis (Verbit and Clark-Lewis, *Tetrahedron*, 24:5519-5527 (1968)); K. Kurosava et al. (Kurosava et al., *Chemical Communications*, 20:1265-1267(1968)); R. Muthyala et al., *Bioorganic and Medicinal Chemistry*, 12:1599-1567 (2004)); K.D.R. Setchell (Setchell, *Fifth International Symposium of the Role of Soy in Preventing and Treating Chronic Disease. Oral Presentation Abstracts*, *American Society for Nutritional Sciences J. Nutr.*, 134:1234S-1247S (2004); and others[1]. These articles support Applicants' assertion that a skilled artisan would understand that a naturally occurring form of equol, as taught by Gorbach, is S-equol.

As such, clearly, the Gorbach reference does not teach administering equol, at least 1% of which is R-equol for mediating androgen hormone action so as to ameliorate at least one condition of the prostate of a subject (as in independent claims 23 and 30). Accordingly, the Gorbach reference simply does anticipate Applicants' independent claims 23 and 30 or any claims dependent therefrom.

The Examiner cited Setchell et al. as evidence that "… the exclusive product of isoflavones is S-equol (abstract)." Applicants note

[1] The above-mentioned articles and additional articles are submitted with an Information Disclosure Statement concomitantly with filing of this Amendment and Response.

that the teachings of Setchell et al. are consistent with Applicants' argument above that because Gorbach only teaches the naturally-occurring plant derived equol, which is S-equol, Gorbach cannot teach compositions comprising equol, at least 1% of which is R-equol.

Applicants request that the anticipation rejection of claims 23, 24, 28, 30, 31, and 33 be withdrawn.

**The § 102 Rejection Based on Setchell and Cole Should Be Withdrawn**

Applicants assert that Setchell and Cole cannot be applied by the Examiner because Setchell and Cole is not prior art under any provisions of §102.

Submitted with Applicants' response is a Declaration of inventor Dr. Edwin Lephart (hereinafter "the Lephart Declaration"). This Declaration provides evidence that the teachings of Setchell and Cole identified by the Examiner in paragraph 16 of the Office action in support of his assertions were, in fact, invented by the inventors named in the instant application prior to the filing date of the Setchell and Cole reference, which is July 24, 2003 and, further, that they were invented by the inventors named in the instant application prior to the filing of the priority document to Setchell et al., Provisional Application No. 60/398,270 (hereinafter "the '270 priority application"), which was filed July 24, 2002.

Specifically, the Lephart Declaration provides evidence that:

a. the inventors named in the instant application, Dr. Edwin Lephart at Brigham Young University, Dr. Trent D. Lund at Colorado State University, Dr. Kenneth David Reginald Setchell from Cincinnati Children's Medical Center, and Dr. Robert J. Handa at Colorado State University, collaborated with the group of Setchell and Cole prior to the filing date of the Setchell and Cole reference and prior to the filing date of the '270 priority application;

b. the subject matter of the instant application was discussed between the inventors named in the instant application prior to the filing date of the Setchell and Cole reference and prior to the filing date of the '270 priority application; and

c. the inventors named in the instant application knew and understood the importance of equol, including its S- and R-enantiomers, and their potential use for prostate health and specifically for the treatment of benign prostatic hyperplasia and prostate cancer, prior to the filing date of Setchell and Cole and prior to the filing date of '270 priority application.

As discussed in the Lephart Declaration, the instant application and the Setchell and Cole reference cited by the Examiner have one inventor in common, namely Dr. Kenneth David Reginald Setchell. Dr. Setchell, Dr. Lephart and the remaining inventors named in instant application collaborated prior to the filing date of the Setchell and Cole reference, as well as, prior to the filing date of the '270 priority application. During this collaboration the inventors discovered that the racemic and non-racemic mixtures of R- and S-enantiomers of equol can be used for prostate conditions.

Exhibit B is a copy of the Colorado State University Disclosure of Invention dated August 6, 2002. This Disclosure of Invention lists four inventors, Dr. Lephart, Dr. Handa, Dr. Lund, and Dr. Setchell, all of whom are also the inventors named in the instant application. At page 1 of the Disclosure of Invention, the date of May 2001 is listed as the date of the first disclosure of the invention described therein to others and the date of first sketch or drawing relating to the invention described therein. The Disclosure of Invention also provides the date of May 30, 2001 as the date of the first written record of the invention described in the Disclosure of Invention. Thus, Exhibit B is evidence of an ongoing collaboration between the inventors named in the instant application, at least from May 2001. All these dates precede the filing date of the Setchell and Cole reference and that of the '270 priority application.

Exhibit B also provides evidence that the inventors named in the instant application knew about equol and its potential applications for prostate health as claimed in the instant application, prior to the filing date of the Setchell and Cole reference and the '270 priority application. Specifically, at page 2 of Exhibit B, under "Brief Summary of the Invention," inventors disclose that equol binds directly to the androgen, 5α-Dihydrotestosterone (5α-DHT). Under "Practical and Commercial Applications," inventors assert that equol may have applications in "… (B) prostate health- benign prostatic hyperplasia (BPH) and prostate cancer… ."

Also, information pertaining R- and S-equol enantiomers was discussed between the inventors named in the instant application prior to the filing date of the Setchell and Cole reference and that of the '270 priority application. Exhibit C is a copy of an e-mail communication between Dr. Lephart and Dr. Lund of June 12th, 2002. In this e-mail communication the inventors discussed collaborative data regarding how equol acts as an anti-androgen and, specifically, 5α-DHT-equol binding data, as well as, the data on equol's effect on body weight, metabolic and cardiovascular parameters and importance of the properties of R- and S-enantiomers of equol. Also, in this e-mail, Dr. Lephart mentioned that he would be sending a draft of a provisional application relating to these findings to Dr. Lund. Later on June 12th, 2002, Dr. Lephart telephoned Dr. Lund to discuss the e-mail communication of June 12th and related matters. Exhibit D is a copy of a telephone bill displaying the record of Dr. Lephart's telephone call to Dr. Lund at the Colorado State University phone number, (970) 491-5638, on June 12th, 2002.

Exhibit E is a copy of Dr. Lephart's personal notes taken during three separate telephone conversations with Dr. Lund on July 10th, 11th and 15th, 2002. On July 10th, 2002 Dr. Lephart and Dr. Lund discussed equol-DHT binding and racemic equol vs. R- and S- enantiomers of equol. On July 11th, 2002 Dr. Lephart and Dr. Lund discussed moving forward with R- and S-equol binding studies. Once more, on July 15th, 2002, Dr. Lephart and Dr. Lund discussed

whether the Colorado State University inventors had the capability of isolating R- and S-equol. Exhibit F is a copy of a telephone bill showing that Dr. Lephart telephoned Dr. Lund at the Colorado State University phone number, (970) 491-5638, on July 10th, 11th, and 15th, 2002.

Exhibit G is a copy of Dr. Lephart's personal notes taken during a telephone conversation with Dr. Setchell on July 17th, 2002. This telephone call lasted for over 2 hours, during which Dr. Lephart and Dr. Setchell discussed DHT-equol binding and, specifically, binding of racemic equol to DHT. The inventors also discussed the R- and S-equol enantiomers and their characteristics, such as activity, estrogenic properties and binding to DHT. Furthermore, the inventors discussed synthesis and isolation of R- and S-equol. Exhibit H is a copy of a telephone bill showing that Dr. Lephart telephoned Dr. Setchell at Cincinnati Children's Medical Center phone number, (513) 636-4548, on July 17th, 2002.

Finally, Exhibit I is a copy of an e-mail communication between Dr. Lephart and Dr. Setchell dated June 07, 2002. In this communication Dr. Lephart informed Dr. Setchell of the finding that equol specifically binds to the DHT-androgen receptor *in vivo* without displacing DHT from the androgen receptor.

In summary, the above-mentioned Lephart Declaration including Exhibits B-H provides evidence that teachings of Setchell and Cole that compositions of equol may include racemic and non-racemic ratios of S-equol to R-equol, and that such compositions may be used for treating and/or ameliorating conditions of the prostate were known and invented by the inventors named in the instant application prior to filing date of the Setchell and Cole reference and prior to the filing date of the '270 priority application. Furthermore, the above-mentioned Lephart Declaration including Exhibits B-H provides evidence that both, R- and S-equol posses the unique anti-androgenic ability to antagonize DHT *in vitro* and *in vivo*, making these compounds promising for treating androgen related diseases were also known and invented by the inventors named in the instant application prior to filing date of the Setchell and Cole reference and prior to the

filing date of the '270 priority application. The Lephart Declaration provides further evidence that the mechanism of action of equol, and specifically that equol antagonizes DHT *in vitro* and *in vivo* was disclosed and known by the inventors named on the instant application prior to the filing date of Setchell and Cole.

Because the subject matter of Setchell and Cole that the Examiner has referred to in his rejection was invented before the filing date of Setchell and Cole and before the filing date of the '270 priority application, this material is not available as prior art under any part of § 102. Applicants request that the Examiner's anticipation rejection of claims 23, 24, 27, 30, 31, and 30 based on Setchell and Cole be withdrawn.

**Rejection under 35 U.S.C. § 103 – Obviousness**

The Examiner rejected claims 23, 29, 30, 34, 38, 42, and 43 under 35. U.S.C.§ 103(a) as being unpatentable over Kelly et al. in view of Luk et al. (Luk et al., Journal of Natural Products, 1983). Specifically, the Examiner asserted that although Kelly et al. teach that equol (compound 10) can be used to treat prostate cancer among other things, Kelly et al. does not teach a non-racemic mixture of equol for treatment of androgen-mediated diseases. The Examiner further asserted that Luk et al. overcomes the deficiencies of Kelly et al. because "Luk, et al. teach that both R- and S-equol were known" and cites page 853, lines 1-3 of Luke et al. to support his assertion. The Examiner concluded that it would have been obvious to one of skill in the art at the time the invention was made to combine the teachings of Kelly et al. and Luk et al. to arrive at methods, as claimed by Applicants.

The rejection of the claims under 35 USC § 103(a) is respectfully traversed. As discussed under the anticipation rejection above, the Kelly et al. reference does not teach, show or even suggest all of the elements of Applicants' rejected independent claims 23 and 30. Specifically, Kelly et al. do not make any

mention of enantiomers of equol and certainly do not teach, show or even suggest *administering compositions comprising equol, at least 1% of which being R-equol*. The cited Luk et al. reference does not overcome the deficiencies of Kelly et al. because nowhere in the Luke et al. reference there is any teaching or suggestion of R-equol. Rather, the Luk et al. reference specifically asserts that:

> "… more recently [equol's] **absolute configuration** was determined to be ***S*** (25-27)." (Luk et al., page 853, lines 2-3; emphases added)

This statement, in turn, supports Applicants' earlier assertion that it was well known at the time of filing of Kelly et al. (and at the time of filing of the previously discussed Gorbach reference, as well as at the time of filing of the instant application) that the naturally occurring form of equol is S-equol (i.e., the form exclusively produced by mammals by intestinal microflora). See, for example, articles by L. Verbit and J.W. Clark-Lewis (Verbit and Clark-Lewis, *Tetrahedron*, 24:5519-5527 (1968)); K. Kurosava et al. (Kurosava et al., *Chemical Communications*, 20:1265-1267(1968)); R. Muthyala et al., *Bioorganic and Medicinal Chemistry*, 12:1599-1567 (2004)); K.D.R. Setchel (Setchel, *Fifth International Symposium of the Role of Soy in Preventing and Treating Chronic Disease. Oral Presentation Abstracts*, *American Society for Nutritional Sciences J. Nutr.*, 134:1234S-1247S (2004); others[2]. Accordingly, Luk et al. confirm that at the time of filing of Applicants' application, the only known configuration of equol was the *S* configuration. Therefore, the Luk et al. reference does not teach administering equol, at least 1% of which is R-equol. Also, nothing in Luk et al. suggests modifying the methods of Kelly et al. to administer equol, at least 1% of which is R-equol, as in Applicants' independent claim 23 and 30.

Moreover, the Examiner has not articulated any reason from the prior art to modify the cited Kelly et al. reference in order to arrive at the claimed methods inasmuch as neither of the applied references even acknowledges or recognizes that conditions of the prostate can be ameliorated by administering equol, at least

[2] The above-mentioned articles and additional articles are submitted with an Information Disclosure Statement concomitantly with filing of this Amendment and Response.

1% of which is R-equol. This teaching is only found in Applicants' disclosure and, in accordance with MPEP 2143, cannot provide a reason to modify or combine references.

Because independent claims 23 and 30 are novel and non-obvious, the methods defined by the claims depending on claims 23 and 30, are also novel and non-obvious. In particular, claims 29 and 34 are not obvious under 35 U.S.C. §103(a) over Kelly et al. and Luk et al. Applicants request that the Examiner's obviousness rejection of claims 23, 29, 30, 34, 38, 42, and 43 be withdrawn.

**Rejection under 35 U.S.C. § 112, First Paragraph – Enablement**

The Examiner rejected claims 23-29 under 35 U.S.C. § 112, First Paragraph, because the specification, while being enabling for treating or reducing the physiological and pathophysiological conditions mediated by androgens comprising administration of equol, does not reasonably provide enablement for enhancing the physiological and pathophysiological conditions mediated by androgens comprising administering equol. The Examiner also rejected claims 30-44 under 35 U.S.C. § 112, First Paragraph, because the specification, while being enabling for treating an androgen-related condition comprising administration of equol, does not reasonably provide enablement for preventing an androgen-related condition comprising administration of equol. The Examiner concluded that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate with these claims.

Applicants disagree with the Examiner. Nonetheless, Applicants amended independent claims 23 and 30 to clarify that these claims are directed to methods of mediating androgen hormone action so as to *ameliorate* at least one condition of the prostate in a subject (claim 23), or methods of *ameliorating* at least one condition of the prostate in a subject (claim 30). In view of the amendment to

independent claims 23 and 30, the 35 U.S.C. § 112, First Paragraph rejection of claims 23 and 30, or any claims dependent therefrom, should be withdrawn.

**Rejection under 35 U.S.C. § 112, Second Paragraph – Indefiniteness**

The Examiner rejected claims 27, 28, 32, and 33 under 35 U.S.C. § 112, Second Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserted that claims 27, 28, 32, and 33 are drawn to a method of treatment comprising the administration of a composition comprising essentially the R-equol (claims 27 and 32) or S-equol (claims 28 and 33) enantiomer. The Examiner concluded that the rejected claims are indefinite because neither the claims nor the specification disclose the meaning of "essentially."

Applicants disagree. Nonetheless, Applicants cancelled claims 27, 28, 32 and 33. In view of the cancellation of claims 27, 28, 32 and 33, the § 112, Second Paragraph rejection of these claims is moot.

## CONCLUSION

Claims 23-25, 29-31, 35, 36, and 45-47 are pending. Applicants respectfully submit that the present application is now in condition for allowance. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned at (312) 245-5398.

Respectfully submitted,

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